

CLAIMS

1. (currently amended) A composition comprising:

- (a) a drug in a pharmaceutically acceptable solubility-improved form; and
- (b) a concentration-enhancing polymer combined with said solubility-improved form in a sufficient amount so that said composition provides, after introduction to a use environment, a maximum concentration of said drug in said use environment that is at least 1.25-fold an equilibrium concentration of said drug in said use environment, and a concentration of said drug in said use environment that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

wherein

said composition is not a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

when said drug is basic, said solubility improved has an aqueous solubility at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid

cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

2. (original) The composition of claim 1 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

3. (withdrawn) The composition of claim 1 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

4. (withdrawn) The composition of claim 1 wherein said drug in said solubility-improved form is amorphous.

5. (withdrawn) The composition of claim 1 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

6. (withdrawn) The composition of claim 5 wherein said solubilizing agent is selected from the group consisting of surfactants, pH control agents, glycerides, partial glycerides, glyceride derivatives, polyoxyethylene and polyoxypropylene ethers and their copolymers, sorbitan esters, polyoxyethylene sorbitan esters, alkyl sulfonates, and cyclodextrins.

7. (withdrawn) The composition of claim 6 wherein said pH control agents are selected from the group consisting of buffers, organic acids, organic acid salts, organic and inorganic bases, and organic and inorganic base salts.

8. (withdrawn) The composition of claim 5 wherein said drug is basic and said solubilizer is an organic acid selected from the group consisting of adipic acid, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid, erythorbic acid, maleic acid, L-aspartic acid, L-glutamic acid, tannic acid, and D,L-tyrosine.

9. (withdrawn) The composition of claim 1 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold said equilibrium concentration of said drug in said use environment.

10. (withdrawn) The composition of claim 9 wherein said liquid is selected from the group consisting of water-immiscible triglyceride vegetable oils, water-immiscible refined and synthetic and semisynthetic oils, mono-, di- and tri-glycerides, water-miscible alcohols, and water-miscible polyethyleneglycols.

11. (withdrawn) The composition of claim 9 wherein said liquid comprises water and a water-soluble solubilizer.

12. (original) The composition of claim 1 wherein said use environment is *in vivo*.

13. (original) The composition of claim 12 wherein said use environment is selected from the group consisting of the GI tract, subcutaneous space, vaginal tract, pulmonary tract, arterial and venous blood vessels, and intramuscular tissue of an animal.

14. (original) The composition of claim 1 wherein said use environment is *in vitro*.

15. (original) The composition of claim 1 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

16. (canceled)

17. (canceled)

18. (previously presented) The composition of claim 1 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

19. (withdrawn) The composition of claim 1 wherein said polymer is a non-ionizable cellulosic polymer.

20. (withdrawn) The composition of claim 19 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

21. (withdrawn) The composition of claim 1 wherein said polymer is an ionizable, non-cellulosic polymer.

22. (withdrawn) The composition of claim 21 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-fuctinoalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

23. (withdrawn) The composition of claim 1 wherein said polymer is a non-ionizable, non-cellulosic polymer.

24. (withdrawn) The composition of claim 23 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

25. (original) The composition of claim 1 wherein said composition provides a dissolution area under the concentration versus time curve in a use environment for a period of at least 90 minutes during the 1200 minutes immediately following introduction to said use environment that is at least 1.25-fold the corresponding area under the curve provided by said control composition.

26. (original) The composition of claim 1 wherein said maximum concentration of said drug in said use environment is at least 2-fold said equilibrium concentration.

27. (original) The composition of claim 1 wherein said composition provides a relative bioavailability of at least 1.25.

28. (original) The composition of claim 1 wherein said composition provides a maximum concentration in said use environment that is at least 1.25-fold the maximum drug concentration in said use environment provided by said control composition.

29. (original) The composition of claim 1 wherein said drug is selected from antihypertensives, antianxiety agents, anticlotting agents, anticonvulsants, blood glucose-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, anti-inflammatories, antipsychotic agents, cognitive enhancers, cholesterol-reducing agents, antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti-depressants, and antiviral agents.

30. (currently amended) A composition comprising:

- (a) a drug in a pharmaceutically acceptable solubility-improved form; and
- (b) a concentration-enhancing polymer combined with said drug in a sufficient amount so that said composition provides, after introduction to a use environment, a dissolution area under the concentration versus time curve in said use environment for a period of at least 90 minutes during the 1200 minutes immediately following introduction to said use environment that is at least 1.25-fold the corresponding area under the curve provided by a control composition, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

wherein

said composition is not a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

when said drug is basic, said solubility improved has an aqueous solubility at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

31. (original) The composition of claim 30 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

32. (withdrawn) The composition of claim 30 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

33. (withdrawn) The composition of claim 30 wherein said drug in said solubility-improved form is amorphous.

34. (withdrawn) The composition of claim 30 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

35. (withdrawn) The composition of claim 34 wherein said solubilizing agent is selected from the group consisting of surfactants, pH control agents, glycerides, partial glycerides, glyceride derivatives, polyoxyethylene and polyoxypropylene ethers and their copolymers, sorbitan esters, polyoxyethylene sorbitan esters, carbonate salts, alkyl sulfonates, and cyclodextrins.

36. (withdrawn) The composition of claim 35 wherein said pH control agents are selected from the group consisting of buffers, organic acids, organic acid salts, organic and inorganic bases, and organic and inorganic base salts.

37. (withdrawn) The composition of claim 34 wherein said drug is basic and said solubilizer is an organic acid selected from the group consisting of adipic acid, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid, erythorbic acid, maleic acid, L-aspartic acid, L-glutamic acid, tannic acid, and D,L-tyrosine.

38. (withdrawn) The composition of claim 30 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold said equilibrium concentration of said drug in said use environment.

39. (withdrawn) The composition of claim 38 wherein said liquid is selected from the group consisting of water-immiscible triglyceride vegetable oils, water-immiscible refined and synthetic and semisynthetic oils, mono-, di-, and tri-glycerides, water-miscible alcohols, and water-miscible polyethyleneglycols.

40. (withdrawn) The composition of claim 38 wherein said liquid comprises water and a water-soluble solubilizer.

41. (original) The composition of claim 30 wherein said use environment is *in vivo*.

42. (original) The composition of claim 41 wherein said use environment is selected from the group consisting of the GI tract, subcutaneous space, vaginal tract, pulmonary tract, arterial and venous blood vessels, and intramuscular tissue of a mammal.

43. (original) The composition of claim 30 wherein said use environment is *in vitro*.

44. (original) The composition of claim 30 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

45. (canceled)

46. (canceled)

47. (previously presented) The composition of claim 30 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

48. (withdrawn) The composition of claim 30 wherein said polymer is a non-ionizable cellulosic polymer.

49. (withdrawn) The composition of claim 48 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

50. (withdrawn) The composition of claim 30 wherein said polymer is an ionizable, non-cellulosic polymer.

51. (withdrawn) The composition of claim 50 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-functionalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

52. (withdrawn) The composition of claim 30 wherein said polymer is a non-ionizable, non-cellulosic polymer.

53. (withdrawn) The composition of claim 52 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

54. (original) The composition of claim 30 wherein said composition provides a maximum concentration of said drug in said use environment that is at least 1.25-fold said equilibrium concentration of said drug provided by said control.

55. (original) The composition of claim 30 wherein said composition provides a relative bioavailability of at least 1.25-fold.

56. (original) The composition of claim 30 wherein said drug is selected from antihypertensives, antianxiety agents, anticlotting agents, anticonvulsants, blood glucose-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, anti-inflammatories, antipsychotic agents, cognitive enhancers, cholesterol-reducing agents, antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti-depressants, and antiviral agents.

57. (original) The composition of claim 30 wherein said drug concentration provided by said composition is greater than the equilibrium concentration of said drug for at least 15 minutes.

58. (currently amended) A composition comprising:

- (a) a drug in a pharmaceutically acceptable solubility-improved form; and
- (b) a concentration-enhancing polymer combined with said drug in a sufficient amount so that said composition provides, after introduction to a use environment, a relative bioavailability of at least 1.25 relative to a control composition that is free from said concentration-enhancing

polymer and comprises an equivalent quantity of said drug in said
solubility-improved form,

wherein

said composition is not a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

when said drug is basic, said solubility improved has an aqueous
solubility at least 2-fold the solubility of the more soluble of the crystalline
hydrochloride salt and the crystalline free base drug form;

said concentration-enhancing polymer is a cellulosic ionizable polymer
selected from the group consisting of cellulose acetate phthalate, methyl
cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl
cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate,
hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate
phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl
cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose
acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate
trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl
cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate
succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate,
cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate
pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid
cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl
ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl
nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic
acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

59. (original) The composition of claim 58 wherein said drug in said
solubility-improved form is a crystalline highly soluble salt form of said drug.

60. (withdrawn) The composition of claim 58 wherein said drug in said
solubility-improved form is a high energy crystalline form of said drug.

61. (withdrawn) The composition of claim 58 wherein said drug in said solubility-improved form is amorphous.
62. (withdrawn) The composition of claim 58 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.
63. (withdrawn) The composition of claim 62 wherein said solubilizing agent is selected from the group consisting of surfactants, pH control agents, glycerides, partial glycerides, glyceride derivatives, polyoxyethylene and polyoxypropylene ethers and their copolymers, sorbitan esters, polyoxyethylene sorbitan esters, carbonate salts, alkyl sulfonates, and cyclodextrins.
64. (withdrawn) The composition of claim 63 wherein said pH control agents are selected from the group consisting of buffers, organic acids, organic acid salts, organic and inorganic bases, and organic and inorganic base salts.
65. (withdrawn) The composition of claim 62 wherein said drug is basic and said solubilizer is an organic acid selected from the group consisting of adipic acid, citric acid, fumaric acid, malic acid, succinic acid, tartaric acid, erythorbic acid, maleic acid, L-aspartic acid, L-glutamic acid, tannic acid, and D,L-tyrosine.
66. (withdrawn) The composition of claim 58 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold said equilibrium concentration of said drug in said use environment.
67. (withdrawn) The composition of claim 66 wherein said liquid is selected from the group consisting of water-immiscible triglyceride vegetable oils, water-immiscible refined and synthetic and semisynthetic oils, mono-, di-, and tri-glycerides, water-miscible alcohols, and water-miscible polyethyleneglycols.
68. (withdrawn) The composition of claim 66 wherein said liquid comprises water and a water-soluble solubilizer.

69. (original) The composition of claim 58 wherein said use environment is *in vivo*.

70. (original) The composition of claim 88 wherein said use environment is selected from the group consisting of the GI tract, subcutaneous space, vaginal tract, pulmonary tract, arterial and venous blood vessels, and intramuscular tissue of an animal.

71. (original) The composition of claim 58 wherein said use environment is *in vitro*.

72. (original) The composition of claim 58 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

73. (canceled)

74. (canceled)

75. (previously presented) The composition of claim 58 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

76. (withdrawn) The composition of claim 58 wherein said polymer is a non-ionizable cellulosic polymer.

77. (withdrawn) The composition of claim 76 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

78. (withdrawn) The composition of claim 58 wherein said polymer is an ionizable, non-cellulosic polymer.

79. (withdrawn) The composition of claim 78 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-fuctinoalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

80. (withdrawn) The composition of claim 58 wherein said polymer is a non-ionizable, non-cellulosic polymer.

81. (withdrawn) The composition of claim 80 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

82. (original) The composition of claim 58 wherein said composition provides a maximum concentration of said drug in said use environment that is at least 1.25-fold said equilibrium concentration of said drug provided by said control.

83. (original) The composition of claim 58 wherein said composition provides a maximum concentration of said drug in said use environment that is at least 2-fold said equilibrium concentration.

84. (original) The composition of claim 58 wherein said drug is selected from antihypertensives, antianxiety agents, anticlotting agents, anticonvulsants, blood glucose-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, anti-inflammatories, antipsychotic agents, cognitive enhancers, cholesterol-reducing agents, antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti-depressants, and antiviral agents.

85. (original) The composition of claim 58 wherein said drug concentration provided by said composition exceeds the equilibrium concentration of said drug for at least 15 minutes.

86. (currently amended) A method of administering a drug comprising co-administering to a patient in need of said drug:

- (a) a drug in a solubility-improved form; and
- (b) a concentration-enhancing polymer;

wherein

said concentration-enhancing polymer is co-administered with said solubility-improved form in a sufficient amount, so that after introduction to a use environment, a maximum concentration of said drug in said use environment is provided that is at least 1.25-fold an equilibrium concentration of said drug in said use environment provided by a control composition;

a concentration of said drug in said use environment is provided that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by said control composition exceeds said equilibrium concentration;

said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

(a) and (b) are not administered in a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

when said drug is basic, said solubility improved has an aqueous solubility at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

87. (original) The method of claim 86 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

88. (withdrawn) The method of claim 86 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

89. (withdrawn) The method of claim 86 wherein said drug in said solubility-improved form is amorphous.

90. (withdrawn) The method of claim 86 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

91. (withdrawn) The method of claim 86 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold an equilibrium concentration of said drug in said use environment.

92. (original) The method of claim 86 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

93. (canceled)

94. (canceled)

95. (previously presented) The method of claim 86 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

96. (withdrawn) The method of claim 86 wherein said polymer is a non-ionizable cellulosic polymer.

97. (withdrawn) The method of claim 96 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

98. (withdrawn) The method of claim 86 wherein said polymer is an ionizable, non-cellulosic polymer.

99. (withdrawn) The method of claim 98 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-fuctinoalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

100. (withdrawn) The method of claim 86 wherein said polymer is a non-ionizable, non-cellulosic polymer.

101. (withdrawn) The method of claim 100 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

102. (original) The method of claim 86 wherein a maximum concentration in said use environment is provided that is at least 1.25-fold the maximum drug concentration in said use environment provided by said control composition.

103. (canceled)

104. (previously presented) The method of claim 86 wherein said drug and said concentration-enhancing polymer are administered at essentially the same time.

105. (original) The method of claim 86 wherein said drug is administered in a composition also comprising said concentration-enhancing polymer.

106. (currently amended) A method of administering a drug comprising co-administering to a patient in need of said drug:

- (a) a drug in a solubility-improved form; and
- (b) a concentration-enhancing polymer;

wherein

said concentration-enhancing polymer is co-administered with said drug in a sufficient amount so that, after introduction to a use environment, a dissolution area under the concentration versus time curve is provided in said use environment for a period of at least 90 minutes during the 1200 minutes immediately following introduction to said use environment that is at least 1.25-fold the corresponding area under the curve provided by a control composition;

said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

(a) and (b) are not administered in a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

when said drug is basic, said solubility improved has an aqueous solubility at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and said drug and said polymer are combined as a simple physical mixture.

107. (original) The method of claim 106 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

108. (withdrawn) The method of claim 106 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

109. (withdrawn) The method of claim 106 wherein said drug in said solubility-improved form is amorphous.

110. (withdrawn) The method of claim 106 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

111. (withdrawn) The method of claim 106 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold an equilibrium concentration of said drug in said use environment.

112. (original) The method of claim 106 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

113. (canceled)

114. (canceled)

115. (previously presented) The method of claim 106 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

116. (withdrawn) The method of claim 106 wherein said polymer is a non-ionizable cellulosic polymer.

117. (withdrawn) The method of claim 106 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

118. (withdrawn) The method of claim 106 wherein said polymer is an ionizable, non-cellulosic polymer.

119. (withdrawn) The method of claim 118 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-fuctinoalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

120. (withdrawn) The method of claim 106 wherein said polymer is a non-ionizable, non-cellulosic polymer.

121. (withdrawn) The method of claim 120 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

122. (original) The method of claim 106 wherein a maximum concentration in said use environment is provided that is at least 1.25-fold the maximum drug concentration in said use environment provided by said control composition.

123. (canceled)

124. (previously presented) The method of claim 106 wherein said drug and said concentration-enhancing polymer are administered at essentially the same time.

125. (original) The method of claim 106 wherein said drug is administered in a composition also comprising said concentration-enhancing polymer.

126. (currently amended) A method of administering a drug comprising co-administering to a patient in need of said drug:

(a) a drug in a solubility-improved form; and

(b) a concentration-enhancing polymer;

wherein

said concentration-enhancing polymer is co-administered with said drug in a sufficient amount so that, after introduction to a use environment, a relative bioavailability is provided of at least 1.25-fold that of a control composition, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form,

(a) and (b) are not administered in a dispersion;

said drug has an aqueous solubility less than about 1 mg/mL;

when said drug is basic, said solubility improved has an aqueous solubility at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form;

said concentration-enhancing polymer is a cellulosic ionizable polymer selected from the group consisting of cellulose acetate phthalate, methyl cellulose acetate phthalate, ethyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, hydroxypropyl methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate succinate, cellulose propionate phthalate, hydroxypropyl cellulose butyrate phthalate, hydroxypropyl methyl cellulose phthalate, hydroxypropyl methyl cellulose acetate succinate, cellulose acetate trimellitate, methyl cellulose acetate trimellitate, ethyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate, hydroxypropyl methyl cellulose acetate trimellitate, hydroxypropyl cellulose acetate trimellitate succinate, cellulose propionate trimellitate, cellulose butyrate trimellitate, cellulose acetate terephthalate, cellulose acetate isophthalate, cellulose acetate pyridinedicarboxylate, salicylic acid cellulose acetate, hydroxypropyl salicylic acid cellulose acetate, ethylbenzoic acid cellulose acetate, hydroxypropyl ethylbenzoic acid cellulose acetate, ethyl phthalic acid cellulose acetate, ethyl nicotinic acid cellulose acetate, carboxymethyl ethyl cellulose and ethyl picolinic acid cellulose acetate; and

said drug and said polymer are combined as a simple physical mixture.

127. (original) The method of claim 126 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

128. (withdrawn) The method of claim 126 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

129. (withdrawn) The method of claim 126 wherein said drug in said solubility-improved form is amorphous.

130. (withdrawn) The method of claim 126 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solubilizing agent.

131. (withdrawn) The method of claim 126 wherein said drug in said solubility-improved form is a solution of a drug substantially dissolved in a liquid to a concentration that is at least 10-fold an equilibrium concentration of said drug in said use environment.

132. (original) The method of claim 126 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

133. (canceled)

134. (canceled)

135. (previously presented) The method of claim 126 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, and cellulose acetate trimellitate.

136. (withdrawn) The method of claim 126 wherein said polymer is a non-ionizable cellulosic polymer.

137. (withdrawn) The method of claim 126 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl cellulose acetate, and hydroxyethyl ethyl cellulose.

138. (withdrawn) The method of claim 126 wherein said polymer is an ionizable, non-cellulosic polymer.

139. (withdrawn) The method of claim 138 wherein said polymer is selected from the group consisting of carboxylic acid functionalized polymethacrylates, carboxylic acid functionalized polyacrylates, amine-functionalized polyacrylates, amine-functionalized polymethacrylates, proteins, and carboxylic acid functionalized starches.

140. (withdrawn) The method of claim 126 wherein said polymer is a non-ionizable, non-cellulosic polymer.

141. (withdrawn) The method of claim 140 wherein said polymer is selected from the group consisting of polyvinyl alcohols that have at least a portion of their repeat units in the unhydrolyzed (vinyl acetate) form, polyvinyl alcohol polyvinyl acetate copolymers, polyethylene glycol, polyethylene glycol polypropylene glycol copolymers, polyvinyl pyrrolidone, polyethylene polyvinyl alcohol copolymers, and chitin.

142. (original) The method of claim 126 wherein a maximum concentration in said use environment is provided that is at least 1.25-fold the maximum drug concentration in said use environment provided by said control composition.

143. (original) The method of claim 126 wherein said drug is administered separately from said concentration-enhancing polymer.

144. (original) The method of claim 143 wherein said drug and said concentration-enhancing polymer are administered at essentially the same time.

145. (original) The method of claim 126 wherein said drug is administered in a composition also comprising said concentration-enhancing polymer.

146. (original) An aqueous solution formed by administration of a solid drug in a solubility-improved form and a concentration-enhancing polymer to a use environment, comprising:

- (a) each of said drug and said concentration-enhancing polymer being at least partially dissolved in said solution;
- (b) at least a portion of said dissolved drug being associated with at least a portion of said polymer in a plurality of assemblies of drug and polymer, said assemblies having a size of from about 10 to 1000 nanometers; and
- (c) said solution having a maximum concentration of said drug that is at least 1.25-fold an equilibrium concentration of said drug in said use environment, and a concentration of said drug that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form.

147. (original) The solution of claim 146 wherein said drug in said solubility-improved form is a crystalline highly soluble salt form of said drug.

148. (withdrawn) The solution of claim 146 wherein said drug in said solubility-improved form is a high-energy crystalline form of said drug.

149. (withdrawn) The solution of claim 146 wherein said drug in said solubility-improved form is amorphous.

150. (withdrawn) The solution of claim 146 wherein said drug in said solubility-improved form is a composition comprising a mixture of said drug and a solid solubilizing agent.

151. (original) The solution of claim 146 wherein said use environment is *in vivo*.

152. (original) The solution of claim 146 wherein said use environment is selected from the group consisting of the GI tract, subcutaneous space, vaginal tract, pulmonary tract, arterial and venous blood vessels, and intramuscular tissue of an animal.

153. (original) The solution of claim 146 wherein said use environment is *in vitro*.

154. (original) The solution of claim 146 wherein said concentration-enhancing polymer has a hydrophobic portion and a hydrophilic portion.

155. (original) An aqueous solution formed by administration of a drug in a solubility-improved form and a concentration-enhancing polymer to a use environment, comprising:

- (a) each of said drug and said concentration-enhancing polymer being at least partially dissolved in said solution;
- (b) at least a portion of said dissolved drug being associated with at least a portion of said polymer in a plurality of assemblies of drug and polymer, said assemblies having a size of from about 10 to 1000 nanometers;
- (c) said polymer being selected from the group consisting of hydroxypropyl methyl cellulose acetate succinate, cellulose acetate phthalate, hydroxypropyl methyl cellulose phthalate, methyl cellulose acetate phthalate, hydroxypropyl cellulose acetate phthalate, cellulose acetate trimellitate, cellulose acetate terephthalate and cellulose acetate isophthalate; and
- (d) said solution having a maximum concentration of said drug that is at least 1.25-fold an equilibrium concentration of said drug in said use environment, and a concentration of said drug that exceeds said equilibrium concentration for a longer time than the concentration of said drug in said use environment provided by a control composition exceeds said equilibrium concentration, wherein said control composition is free from said concentration-enhancing polymer and comprises an equivalent quantity of said drug in said solubility-improved form.

156. (previously added) The composition of claim 1, wherein said drug is ziprasidone.
157. (previously added) The composition of claim 30, wherein said drug is ziprasidone.
158. (previously added) The composition of claim 58, wherein said drug is ziprasidone.
159. (previously added) The method of claim 86, wherein said drug is ziprasidone.
160. (previously added) The method of claim 106, wherein said drug is ziprasidone.
161. (previously added) The method of claim 126, wherein said drug is ziprasidone.
162. (previously added) The solution of claim 146, wherein said drug is ziprasidone.
163. (previously added) The solution of claim 155, wherein said drug is ziprasidone.